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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/963,656	11/03/1997	CRAIG J. GERARD	KS9405A2Z	1351

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EXAMINER
MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	08/963,656	GERARD ET A.
	Examiner	Art Unit
	Joseph F Murphy	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *151-220,246-266 and 292-356* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *300-307* is/are allowed.

6)☒ Claim(s) *151-220, 246-266, 292-299, 308-356* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 221-245 and 267-291 were canceled, and claims 151-157, 163-169, 175-179, 185-188, 194-198, 204-207, 213, 217, 246-250, 253, 257-260, 263, 292, 296, 300 and 300 were amended and new claims 308-356 were added in Paper No. 29, 4/11/2003. Claims 246, 253, 257, 263, 341, 346 and 349 were amended in Paper No. 31, 6/26/2003. Claims 151-220, 246-266, 292-356 are pending and under consideration.

Response to Amendment

Applicant's amendment and arguments filed in Paper No. 29, 4/11/2003 and Paper No. 31, 6/26/2003 have been fully considered, but they are persuasive in part.

The rejections of claims 221-245 and 267-291 have been rendered moot by cancellation of the claims.

The rejection of claims 151-307 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for recitation of the term "naturally occurring" has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claims 303-307 under 35 U.S.C. 103(a) as being unpatentable over WO 94/11504 (Horuk et al.) in view of U.S. Patent No. 5,530,101 (Queen et al.) has been withdrawn based on Applicant's arguments.

New issues and remaining issues are set forth below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 151-158, 160-166, 168-170, 172-176, 178-180, 182-189, 191-195, 197-199, 201-208, 210-220, 246-257, 253-261, 263-266, 292-299, 308-310, 313-315, 317-322, 325-327, 329-336, 338-343, 345-347, 349-356 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 94/11504 (Horuk et al.).

The reference of Horuk et al. teaches the cloning and expression of the C-C chemokine receptor (CKR-1) ('504 at 2). Horuk et al. teaches polyclonal antibodies to CKR-1 on page 39. Horuk et al. teaches monoclonal antibodies on page 40, as well as hybridoma production. Also disclosed are antibodies which antagonize CKR-1 activity or binding. The antibodies which bind CKR-1 would bind the amino acid sequence set forth in the instant application as SEQ ID NO: 4 (See Sequence Comparison A, attached) as well as to the amino acid sequence set forth in the instant application as SEQ ID NO: 6 (see Sequence Comparison B, attached). It is an inherent property of antibodies to CKR-1 to compete with antibodies to the amino acid sequence set forth as SEQ ID NO: 4 or 6, because they would be competing for the same binding site. The polynucleotide which encodes CKR-1 would hybridize under the conditions listed in the relevant claims to the nucleic acid of SEQ ID NO: 3 or 5. The CKR-1 polypeptide binds RANTES, and

other C-C ligands, thus claims 151-158, 160-166, 168-170, 172-176, 178-180, 182-189, 191-195, 197-199, 201-208, 210-220, 246-257, 253-261, 263-266, 292-299, 308-310, 313-315, 317-322, 325-327, 329-336, 338-343, 345-347, 349-356 are anticipated.

Claims 167, 175-177, 179-180, 182-184, 187-189, 194-196, 206-208, 213-216, 246-248, 250-251, 253-261, 292-295, 308-312, 314-315, 317-324, 326-327, 329-336, 338-344, 346-347, 349-353, 355 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,707,815 (Charo et al.).

The '815 patent discloses human chemokine receptor proteins MCP-1RA and MCP-1RB, which are substantially free from other mammalian proteins with which they are typically found in their native state (column 3, lines 10-15). Also disclosed are antibodies to MCP-1RA and MCP-1RB (column 16, lines 15-18). The antibodies to MCP-1RA or B would bind the amino acid sequence set forth as SEQ ID NO: 2 in the instant application (see Sequence Comparison C, attached). The polynucleotide which encodes MCP-1RA or B would hybridize under the conditions listed in the relevant claims to the nucleic acid of SEQ ID NO: 3, thus claims 167, 175-177, 179-180, 182-184, 187-189, 194-196, 206-208, 213-216, 246-248, 250-251, 253-261, 292-295, 308-312, 314-315, 317-324, 326-327, 329-336, 338-344, 346-347, 349-353, 355 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,707,815 are rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 151-154, 156-166, 168-176, 178-195, 197-224, 226-247, 249-270, 272-299, 303-307 stand rejected, and new claims 308-310, 313-356 are rejected, under 35 U.S.C. 103(a) as being unpatentable over WO 94/11504 (Horuk et al.) in view of U.S. Patent No. 5,530,101 (Queen et al.), for reasons of record set forth in Paper No. 27, 10/8/2002.

The rejection of record set forth that the reference of Horuk et al. teaches the cloning and expression of the C-C chemokine receptor (CKR-1) ('504 at 2). Horuk et al. teaches polyclonal antibodies to CKR-1 on page 39. Horuk et al. teaches monoclonal antibodies on page 40, as well as hybridoma production. Also disclosed are antibodies which antagonize CKR-1 activity or binding. The antibodies which bind CKR-1 would bind the amino acid sequence set forth in the instant application as SEQ ID NO: 4 (See Sequence Comparison A, attached) as well as to the amino acid sequence set forth in the instant application as SEQ ID NO: 6 (see Sequence Comparison B, attached). It would be an expected property of antibodies to CKR-1 to compete with antibodies to the amino acid sequence set forth as SEQ ID NO: 4 or 6, because they would be competing for the same binding site. The polynucleotide which encodes CKR-1 would hybridize under the conditions listed in the relevant claims to the nucleic acid of SEQ ID NO: 3 or 5. The CKR-1 polypeptide binds RANTES, and other C-C ligands. Horuk et al. does not teach humanized antibodies, chimeric antibodies or antigen-binding fragments.

U.S. Patent No. 5,530,101 teaches methods for preparing humanized immunoglobulin chains having generally one or more complementarity determiningregions (CDR's) from a donor immunoglobulin and a framework region from a human immunoglobulin. (column 2, lines 35-40). The '101 patent also teaches the immunoglobulins, including binding fragments and other immunoglobulin forms, of the present invention may be produced readily by a variety of recombinant DNA or other techniques. Preferably, polynucleotides encoding the desired amino acid sequences are produced synthetically and by joining appropriate nucleic acid sequences, with ultimate expression in transfected cells (column 3, lines 43-50). Thus, it would have been obvious to one of skill in the art at the time the invention was made to produce humanized or chimeric antibodies to the CKR-1 polypeptide, which would also bind the polypeptides disclosed as SEQ ID NO: 4 and 6. The motivation is provided in the '101 patent which discloses that there is a need for improved forms of human-like immunoglobulins specific for a predetermined antigen that are substantially non-immunogenic in humans, yet easily and economically produced in a manner suitable for therapeutic formulation and other uses (column 2 lines 25-32).

Applicant argues that the claims are not obvious because the regions of sequence identity are found in the transmembrane and/or the intracytoplasmic domains of the proteins. Applicant further argues that sequences that are within the transmembrane and/or the intracytoplasmic domains of the target proteins are not available for antibody binding when the CCR-3 protein is expressed on the surface of a cell. However, the claims do not contain a limitation wherein the claimed antibody is targeted only to the polypeptides of SEQ ID NO: 2 or 4 when they are expressed on the cell surface. The claims are directed to antibodies which bind the polypeptides, and are independent of the milieu in which the proteins are expressed. The antibodies which are

disclosed in the Horuk reference which are directed to the CCR1 and CCR2 would be expected to bind the polypeptides of SEQ ID NO: 4 or 6 if the polypeptides were isolated from the cell membrane, or if the polypeptides were expressed using an in vitro translation system, for example. The claims encompass antibodies to the CCR3 polypeptides in both these situations, and thus the claims are obvious.

Claims 151, 155, 157-162, 167, 175-177, 179-184, 194-196, 198-203, 212-216, 221-225, 228-233, 238-241, 246-248, 250-256, 259-262, 267-271, 273-279, 284-287, 292-295, 303-307 stand rejected, and new claims 308-312, 314-324, 332-356 are rejected, under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,707,815 (Charo et al.) in view of U.S. Patent No. 5,530,101 (Queen et al.), for reasons of record set forth in Paper No. 27, 10/8/2002.

The '815 patent discloses human chemokine receptor proteins MCP-1RA and MCP-1RB, which are substantially free from other mammalian proteins with which they are typically found in their native state (column 3, lines 10-15). Also disclosed are antibodies to MCP-1RA and MCP-1RB (column 16, lines 15-18). The antibodies to MCP-1RA or B would bind the amino acid sequence set forth as SEQ ID NO: 2 in the instant application (see Sequence Comparison C, attached). The polynucleotide which encodes MCP-1RA or B would hybridize under the conditions listed in the relevant claims to the nucleic acid of SEQ ID NO: 3. The 815 patent does not teach humanized antibodies, chimeric antibodies or antigen-binding fragments.

U.S. Patent No. 5,530,101 teaches methods for preparing humanized immunoglobulin chains having generally one or more complementarity determiningregions (CDR's) from a donor immunoglobulin and a framework region from a human immunoglobulin. (column 2, lines 35-

40). The '101 patent also teaches the immunoglobulins, including binding fragments and other immunoglobulin forms, of the present invention may be produced readily by a variety of recombinant DNA or other techniques. Preferably, polynucleotides encoding the desired amino acid sequences are produced synthetically and by joining appropriate nucleic acid sequences, with ultimate expression in transfected cells (column 3, lines 43-50). Thus, it would have been obvious to one of skill in the art at the time the invention was made to produce humanized or chimeric antibodies to the MCP1RA or B polypeptide which would also bind the polypeptide disclosed as SEQ ID NO: 2. The motivation is provided in the '101 patent which discloses that there is a need for improved forms of human-like immunoglobulins specific for a predetermined antigen that are substantially non-immunogenic in humans, yet easily and economically produced in a manner suitable for therapeutic formulation and other uses (column 2 lines 25-32).

Applicant argues that the claims are not obvious because the regions of sequence identity are found in the transmembrane and/or the intracytoplasmic domains of the proteins. Applicant further argues that sequences that are within the transmembrane and/or the intracytoplasmic domains of the target proteins are not available for antibody binding when the CCR-3 protein is expressed on the surface of a cell. However, the claims do not contain a limitation wherein the claimed antibody is targeted only to the polypeptides of SEQ ID NO: 2 or 4 when they are expressed on the cell surface. The claims are directed to antibodies which bind the polypeptides, and are independent of the milieu in which the proteins are expressed. The antibodies which are disclosed in the Horuk reference which are directed to the CCR1 and CCR2 would be expected to bind the polypeptides of SEQ ID NO: 2 if the polypeptides were isolated from the cell membrane, or if the polypeptides were expressed using an in vitro translation system, for

example. The claims encompass antibodies to the CCR3 polypeptides in both these situations, and thus the claims are obvious.

Conclusion

Claims 300-307 are allowable.

Claims 151-220, 246-266, 292-299, 308-356 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
September 5, 2003

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